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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Heather J. Jordan

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EXAMINER

SISSON, BRADLEY L

ART UNIT

PAPER NUMBER

1634

MAIL DATE

DELIVERY MODE

05/27/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 09/613,903	Applicant(s) JORDAN, HEATHER J.	
	Examiner Bradley L. Sisson	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 May 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 141, 150, 155-160 and 162-173 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 141, 150, 155-160 and 162-173 is/are rejected.
- 7) ☒ Claim(s) 150, 155-160 and 162-164 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 27 October 2000 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>13 May 2009</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 04 may 2009 has been entered.

Claim Objections

2. Claims 150, 155-160 and 162-163 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Each of claims 150, 155-160 and 162-163 depends from independent claim 141. Claim 141 was amended to recite the limitation that it "consists of" those elements recited in claim 141. Claims 150, 155-160 and 162-163 seek to introduce new elements and in numerous cases, use the expression "comprises," which opens up the claims to include a limitless number of additional, unidentified components. Accordingly, claims 150, 155-160 and 162-163 do not further limit claim 141 from which they depend.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 141, 150, 155-160, 162-164, 166-168 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claim 141 has been amended to now recite that the nucleic acid ladder “consists” of a plurality of double stranded nucleic acid fragments. Said claim 141, however, still retains multiple usage of the term “comprising” to define the possible fragments. The presence of both consisting and comprising in the same sentence leaves the metes and bounds of the claim in doubt. Claims 150, 155-160, and 162-164, which depend from claim 141 fail to overcome this issue and are similarly rejected. It is further noted, for example, that claim 156 uses the term “comprises” and claim 157 identifies additional components of the nucleic acid ladder, components that seemingly would be excluded by one reading of claim 141.

6. As presently worded, claim 141 makes reference to the “relative mass” of a fragment of nucleic acids and, in part, defines it in term of the copy number of a given fragment. This asserted relationship is confusing as a fragment has mass on its own. Having more of a given fragment does not alter the mass of the individual molecules. Seemingly, applicant is attempting to make reference to the mass of a band in a gel; however, the claimed invention is not part of a gel. Indeed, by applicant using the term “consisting of,” the DNA fragments have been construed as being in a desiccated state.

7. Newly added claim 166 is written such that it depends from self, not any preceding claim. Accordingly, it is not readily apparent just what the limitations the claim is to comprise. Claims

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167 and 168, which depend from claim 166, fail to overcome this issue and are similarly rejected.

8. Claim 169 is indefinite with respect to what constitutes a “highlighted fragment.” Claims 17-173, which depend from said claim 169, fail to overcome this issue and are similarly rejected.

9. Claim 169 is indefinite in that in one instance it specifies that the relative mass of the fragments cannot be more than 3 times that of any other fragment, yet the same composition is to “comprise” highlighted fragments that is more than 3x the relative mass of the other fragments. Accordingly, the claim seemingly has broader and narrower limitation that fall within the broader limitations.

Claim Rejections - 35 USC § 101

10. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

11. Claims 150, 155, 165-173 rejected under 35 U.S.C. 101 because the disclosed invention is inoperative and therefore lacks utility. Claims 150 and 155 each depend from independent claim 141. Claim 141 specifies that the fragments cannot be more than 3 times the mass of any other fragment. Claim 150 and 155 require that there be at least 3 of 4 fragments having a size greater than 1 kb and that there be at least 3 (claim 150) or 4 (claim 155) fragments having a size less than 1 kb. Such breadth of scope has been construed to encompass fragments that are, for example, 100 base pairs long, 200 base pairs long, 300 base pairs long, and 400 base pairs long, as well as fragments that are 2 kb long, 3 kb long, 4 kb long, and 5 kb long. Clearly, the 2 kb fragment would have a relative mass that is more than 3x the mass of the 400 bp fragment.

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12. Accordingly, a composition comprising the fragments recited in claims 150 and 155 is not possible to achieve with respect to the factor of 3x mass limitation required in claim 141.

13. Claim 165 requires that one select 3 or more fragments from one group and 3 or more fragments from a second group, and stipulates that the mass of more fragment cannot be more than 3x that of another fragment. The smallest fragment in the first group is 100 base pairs and the smallest of the second group is 1 kb. Clearly, the mass of a 1 kb fragment is 10x that of the 100 bp fragment. Claims 166-168, which have been construed as depending from claim 165, do not overcome this issue and are similarly rejected.

14. Independent claim 169, recites the same requirements as does independent claim 165 in terms of groupings, sizes of fragments to select from, and relative mass requirements. Claims 170-173, which depend from claim 169, fail to overcome this issue and are similarly rejected.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

16. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

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4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

17. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

18. Claims 141, 150, 155-157 and 159-160, 162-164 are rejected under 35 U.S.C. 103(a) as obvious over either US Patent 5,316,908 (Carlson et al.) or Stratagene (1993) or Stratagene Catalog (1993).

19. As a result of amendment, claim 141 has been amended so to recite the clause "consisting of" a plurality of double stranded nucleic acid fragments." Said claim also recites on two occasions the expression "the plurality [of fragments] comprises." Accordingly, the claim has been construed as encompassing components in addition to the required fragments.

20. For purposes of examination, the claims have been construed as encompassing nucleic acid fragments that manifest as "discrete bands of substantially equal intensity...when the fragments are resolved on a gel and stained" (specification at page 6, first full paragraph).

21. Carlson et al., Fig. 1, disclose a nucleic acid ladder that comprises multiple nucleic acid fragments that have the same intensity. As seen in the figure, below, there are 5 bands that are less than 1 kb and there are at least four bands that have greater than 1 kb in mass.

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22. It is noted with particularity that a compound and its properties are inseparable. While one may identify new properties or new means for evaluating same, such does not make an old compound, or old composition, new and patentable. The claims recite no chemical or physical component that would make the nucleic acid of the claims any different from the nucleic acid ladders of the prior art. Indeed, page 8, fifth paragraph, of the specification states in part:

“However, any nucleic acid molecule or combination of molecules may be used to produce the ladders or compositions of the invention.”

23. While Fig. 1 is a drawing and not a photograph, the specification does state that the Figure does represent the migration of the nucleic acid ladder in an electrophoretic environment. Said Figure clearly shows that the bands have the same relative intensity.

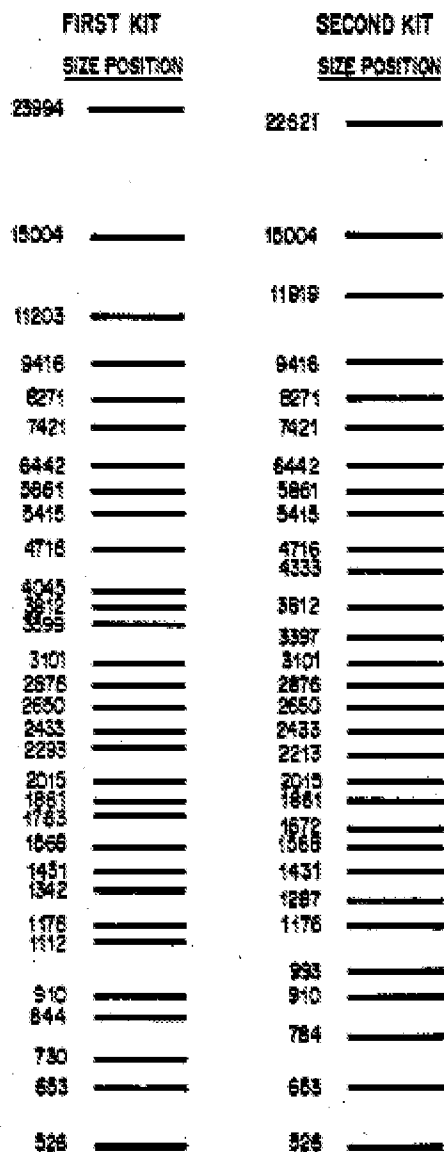


FIG.1

24. To the extent that claim 159 does positively recite that the ladder is stained with ethidium bromide, it is noted that Carlson et al. disclose such, at column 4. For purposes of examination, ethidium bromide is construed to meet the requirements of a dye as it is typically used to stain the entire gel, and with it, stain (dye) preferentially the nucleic acids therein. Accordingly, a limitation of claims 157, 159, and 160 are deemed to be met by the disclosure of Carlson et al.

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25. Carlson et al., disclose nucleic acid ladders that comprise numerous bands that span a wide range of fragment sizes. While some of the rungs of the nucleic acid ladder fall within the recited ranges of claims, the disclosed nucleic acid ladders also comprise additional nucleic acid fragments that are outside of the recited range. Such additional bands do not detract from the instant rejection as the claims, through the use of the term “comprising,” (claim 141, lines 8 and 9) allows for the inclusion of additional reagents (rungs of a ladder), even in significant amounts.

26. The claims do not recite any material difference in the composition of nucleic acid individual fragments. Further, there is no specific wording as to the copy number of the fragments of any given size, or combination of sizes.

27. While newly presented claims have language directing to how the relative mass is to be calculated, it is noted that the instant claims are drawn to a composition, not to a method. Accordingly, the same composition, defined by other terms, can and does anticipate the claimed invention. In support of this position, attention is directed to page 6 of the disclosure which states in part:

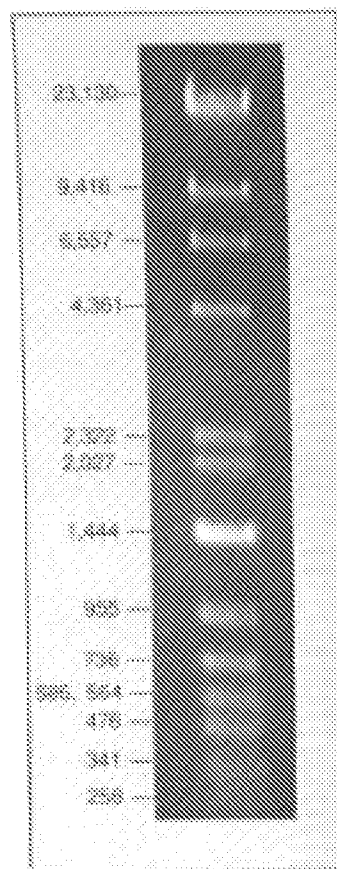
Preferably, the relative mass of each different sized fragment is substantially equivalent such that discrete bands of substantially equal intensity are produced when the fragments are resolved on a gel and stained.

28. Stratagene, at page T22, disclose a Lambda/Hind III nucleic acid ladder. As seen in the image, the ladder comprises multiple fragments that appear to have “substantially equal intensity.” The ladder clearly comprises at least two fragments larger than 1 kb and two fragments less than 1 kb which have “substantially equal intensity.” Given that a compound and its properties are inseparable, and given applicants statement that nucleic acid fragments that

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have “substantially equivalent intensities” also have substantially equivalent relative mass (*supra*), the fragments of Stratagene are deemed to anticipate the claimed nucleic acid ladder.

29. To the degree that claims 142-156 define alternative ranges of the fragment sizes, the nucleic acid fragments of Stratagene clearly fall within each of the stated ranges. Accordingly, the DNA ladder of Stratagene is deemed to meet a limitation of each of said claims.



30. The selection of which band or combination of bands, and their relationship to one another, is not deemed to constitute a patentable distinction over the prior art. Rather, such limitations are deemed to be the result of design choice and/or routine optimization.

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31. It is well settled that routine optimization is not patentable, even if it results in significant improvements over the prior art. In support of this position, attention is directed to the decision in *In re Aller, Lacey, and Hall*, 105 USPQ 233 (CCPA 1955):

Normally, it is to be expected that a change in temperature, or in concentration, or in both, would be an unpatentable modification. Under some circumstances, however, changes such as these may impart patentability to a process if the particular ranges claimed produce a new and unexpected result which is different in kind and not merely in degree from the results of the prior art. In *re Dreyfus*, 22 C.C.P.A. (Patents) 830, 73 F.2d 931, 24 USPQ 52; In *re Waite et al.*, 35 C.C.P.A. (Patents) 1117, 168 F.2d 104, 77 USPQ 586. Such ranges are termed "critical" ranges, and the applicant has the burden of proving such criticality. In *re Swenson et al.*, 30 C.C.P.A. (Patents) 809, 132 F.2d 1020, 56 USPQ 372; In *re Scherl*, 33 C.C.P.A. (Patents) 1193, 156 F.2d 72, 70 USPQ 204. However, even though applicant's modification results in great improvement and utility over the prior art, it may still not be patentable if the modification was within the capabilities of one skilled in the art. In *re Sola*, 22 C.C.P.A. (Patents) 1313, 77 F.2d 627, 25 USPQ 433; In *re Normann et al.*, 32 C.C.P.A. (Patents) 1248, 150 F.2d 708, 66 USPQ 308; In *re Irmscher*, 32 C.C.P.A. (Patents) 1259, 150 F.2d 705, 66 USPQ 314. More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. In *re Swain et al.*, 33 C.C.P.A. (Patents) 1250, 156 F.2d 239, 70 USPQ 412; *Minnesota Mining and Mfg. Co. v. Coe*, 69 App. D.C. 217, 99 F.2d 986, 38 USPQ 213; *Allen et al. v. Coe*, 77 App. D. C. 324, 135 F.2d 11, 57 USPQ 136. (Emphasis added)

32. The plurality of bands that make up each rung in the ladder of Carlson et al., and of Stratagene are deemed to have "substantially relative equal mass" as the band is shown to have "substantially equal intensities" after being separated as bands on a gel and stained.

Accordingly, claims 141, 150, 155-157 and 159-160, 162-164 are rejected under 35

U.S.C. 103(a) as obvious over either US Patent 5,316,908 (Carlson et al.) or Stratagene (1993) or Stratagene Catalog (1993).

33. Claim 158 is rejected under 35 U.S.C. 103(a) as being unpatentable over either US Patent 5,316,908 (Carlson et al.) or Stratagene (1993) or Stratagene Catalog (1993) when taken in view of US Patent 5,635,365 (Ansari et al.).

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34. See above for the basis of the rejection as it relates to the disclosure of both Carlson et al., and Stratagene.

35. Neither Carlson et al., nor Stratagene have been found to disclose staining the ladders with SYBR green ([2-[N-(3-dimethylaminopropyl)-N-propylamino]-4-[2,3-dihydro-3-methyl-(benzo-1,3-thiazol-2-yl)-methylidene]-1-phenyl-quinolinium]⁺).

36. Ansari et al., column 15, third paragraph, teaches explicitly of staining a gel with SYBR green so to enable visualization of the nucleic acid fragments separated therein.

37. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the nucleic acid ladders of either Carlson et al., or Stratagene with SYBR green as disclosed by Ansari et al., as such would have allowed the ordinary artisan with an easy, sensitive and reproducible means for detecting nucleic acids. In view of the detailed teachings in the prior art, said ordinary artisan would have had a most reasonable expectation of success.

38. For the above reasons, and in the absence of convincing evidence to the contrary, claim 158 is rejected under 35 USC 103(a) as being unpatentable over either US Patent 5,316,908 (Carlson et al.) or Stratagene (1993) or Stratagene Catalog (1993) when taken in view of US Patent 5,635,365 (Ansari et al.).

Conclusion

39. Objections and/or rejections which appeared in the prior Office action and which have not been repeated hereinabove have been withdrawn.

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40. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751.

The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

41. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

42. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Bradley L. Sisson/
Primary Examiner, Art Unit 1634